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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/538,885 | 03/29/2006 | Craig L. Nessler | 01640421AA | 8840 |
| 30743 | 7590 | 12/11/2007 | EXAMINER | |
| WHITHAM, CURTIS & CHRISTOFFERSON & COOK, P.C. 11491 SUNSET HILLS ROAD SUITE 340 RESTON, VA 20190 | | | BAGGOT, BRENDAN O | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | |
|------------------------------|------------------------|---------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 10/538,885 | NESSLER ET AL. |
| | Examiner | Art Unit |
| | Brendan O. Baggot | 1638 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 20 August 2007.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-23 is/are pending in the application.
 - 4a) Of the above claim(s) 1-12, 17, 18 and 21-23 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 13-16, 19 and 20 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 6/14/05
- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____

DETAILED ACTION

Restriction / Election

1. Applicant timely traversed the restriction (election) requirement in the reply filed on 8/20/07.
2. Claims 1-12, 17-18, 21-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/20/07.
3. Claim 13-16 and 19-20 are pending and examined in the instant application.

Specification

4. Applicant is required to update the status (pending, allowed, etc.) of all parent priority applications in the first line of the specification. The status of all citations of US filed applications in the specification should also be updated where appropriate. See MPEP 201.11, MPEP 601(I).
5. The use of the trademark BD-Talon® has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

6. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless

the references have been cited by the examiner on form PTO-892, they have not been considered.

7. The text “Figures 3 and 4” on page 13, last line, 1st paragraph should be amended to Figures 4 and 5 so as to correctly refer to the Figures discussed therein.

Claim Objections

8. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claims 14 and 15 depending from claim 13 lack antecedent basis for the term “plant.”.

9. Claims 14 and 15 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims are directed to product claims but depend from a method claim. See MPEP § 608.01

Claim Interpretation

A claim limitation will be presumed to invoke 35 U.S.C. 112, sixth paragraph, if it meets the following 3-prong analysis:

- (A) the claim limitations must use the phrase “means for ” or “step for; ”
- (B) the “means for ” or “step for ” must be modified by functional language; and
- (C) the phrase “means for ” or “step for ” must not be modified by sufficient structure, material, or acts for achieving the specified function.

With respect to the first prong of this analysis, a claim element that does not include the phrase “means for” or “step for” will not be considered to invoke 35 U.S.C. 112,

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sixth paragraph. If an applicant wishes to have the claim limitation treated under 35 U.S.C. 112, sixth paragraph, applicant must either: (A) amend the claim to include the phrase "means for" or "step for" in accordance with these guidelines; or (B) show that even though the phrase "means for" or "step for" is not used, the claim limitation is written as a function to be performed and does not recite sufficient structure, material, or acts which would preclude application of 35 U.S.C. 112, sixth paragraph. Where a method claim does not contain the term "steps for", a limitation of that claim cannot be construed as a step-plus-function limitation without a showing that the limitation contains no act. See MPEP 2181.

Because claim 15 does not contain the phrase "means for," claim 15 fails the must use the phrase "means for" or "step for" prong recited above and therefore has not been interpreted as a means plus function claim.

Claim Rejections - 35 USC § 112, 1st, paragraph, written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 13-16, 19-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of reducing TSNAs in tobacco with at least one gene in a Vitamin C biosynthetic pathway. Applicants recite a method of increasing endogenous Vitamin C by transforming plants with At-MIOX4. Applicants do not describe a method of reducing TSNAs in tobacco with at least one gene in a Vitamin C biosynthetic pathway.

Applicants fail to describe a representative number of members of the claimed genus of Vitamin C pathway enzymes. There is no clear depiction of any Vitamin C pathway enzyme of any length and sequence from any source. The disclosed species are not representative of the claimed genus because Applicants describe one example of GLOase and one example of MIOX. No examples of any of the rest of the genes in the pathway are provided. The Vitamin C pathway is not well understood in plants. There are thought to be 10-20 different enzymes in the plant Vitamin C pathway. A single example of just two of the many pathway enzymes, without a description of the structural features essential for function of each and every enzyme required, is not representative of all and any Vitamin C pathway enzyme of any length and sequence from any source.

Furthermore, Applicants fail to describe structural features common to members of the claimed genus of Vitamin C pathway enzymes. Furthermore, given the lack of description of the necessary elements essential for Vitamin C pathway enzymes, it remains unclear what features identify Vitamin C pathway enzymes. Since the genus of Vitamin C pathway enzymes has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

Moreover, six months after the instant filing date applicants themselves teach that “[t]here are . . . two enzymatic reactions required for the conversion of d-glucuronate, the

MIOX4 product, to L-GulL. The initial reaction is most likely catalyzed by an aldehyde reductase (E.C. 1.1.1.19); however, there are no reports in the literature regarding the characterization of such an enzyme in plants. (Lorenz, 2004, Plant Physiol. 134:1200-1205; 1203, right col. 2nd to last parag.). Thus it appears that at least some enzymes in the pathway were unknown at the time of filing.

Given the claim breadth and lack of guidance as discussed above, the specification fails to provide an adequate written description of the genus of any genes within the Vitamin C pathway enzyme of any length and sequence from any source. Given the lack of written description of the claimed genus of sequences, any method of using them, such as transforming plant cells and plants therewith, and the resultant products including the claimed transformed plants containing the genus of sequences, would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicant to have been in possession of the claimed invention at the time of filing. *See The Written Description Requirement guidelines published in Federal Register/ Vol. 66, No. 4/ Friday January 5, 2001/ Notices: pp. 1099-1111.*

Claim Rejections - 35 U.S.C. §112, first paragraph, enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 13-16, 19-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing endogenous Vitamin C by transforming plants with At-MIOX4, does not reasonably provide enablement for reducing

TSNAs in tobacco with at least one gene in a Vitamin C biosynthetic pathway. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The *Wands* court set forth the enablement balancing test:

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). *Wands* states at page 1404, “Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the ‘claims.’”

M.P.E.P. § 2164.01(a).

The claims are to a method of reducing TSNAs in tobacco with at least one gene in a Vitamin C biosynthetic pathway. Applicants teach a method of increasing endogenous Vitamin C by transforming plants with At-MIOX4. Applicants do not teach a method of reducing TSNAs in tobacco with at least one gene in a Vitamin C biosynthetic pathway.

The state-of-the-art is such that one of skill in the art cannot predict what the sequence of every Vitamin C pathway enzyme is. “Experiments are in progress to clone and characterize the remaining members of the MIOX family and to test the potential contribution of each member to Ascorbic Acid (AsA) biosynthesis.” Moreover, there are no reports in the literature regarding the characterization of one [Vitamin C]pathway enzyme[,] aldehyde reductase. (Lorenz, 2004, Plant Physiol. 134:1200-1205, page 1204, left col., 3d parag.). Thus it appears that at least some enzymes in the pathway were unknown at the time of filing. As of the filing date of the

application, it was even less predictable and more experimental to determine what the sequence of every Vitamin C pathway enzyme is.

The specification, while suggesting the use of At-MIOX4 and rat L-gulono- γ -lactone oxidase (GLOase), does not provide significant guidance on how to overcome art recognized problems in identifying genes which were unknown 6 months after the filing of the instant application.

Without sufficient guidance, determination of the sequence of any Vitamin C pathway enzyme of any length and sequence from any source is unpredictable. Without guidance on how to overcome the difficulty in identifying unknown genes in plants, determination of the sequence of any Vitamin C pathway enzyme of any length and sequence from any source is unpredictable and the experimentation left to those skilled in the art is undue.

Therefore, given the breadth of the claims; the lack of guidance and working examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue trial and error experimentation would be required to practice the claimed invention, and therefore the invention is not enabled throughout the broad scope of the claims.

Claim Rejections - 35 U.S.C. §102, lack of novelty

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

35 U.S.C. §102.

12. Claims 13-15 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Jain et al (2000. Metabolic engineering of an alternative pathway for ascorbic acid biosynthesis in plants, Molecular Biology 6:73-78).

Jain discloses a method for reducing TSNAs in air cured tobacco, comprising the step of genetically engineering said tobacco (page 74, paragraph bridging col. 1 and 2) to include not a myo-inositol oxidase (MIOX) but instead a L-gulono- γ -lactone oxidase (GLOase, see abstract, GLOase is a gene in a vitamin C biosynthetic pathway) wherein said step of genetically engineering said tobacco results in reduced levels of TSNAs in said tobacco, wherein said tobacco inherently includes more than one copy of said gene, wherein said tobacco further includes a means to enhance transcription of said gene or genes (via a promoter, page 74, left column, 2nd Para.), wherein said step of genetically engineering said tobacco results in an increase in an endogenous level of vitamin C in said tobacco.

Because multiple copies are routinely seen in plants transformed via *Agrobacterium-mediated* transformation, the plants of Jain would inherently have multiple copies of the gene. Thus, the reference discloses all the limitations of the Claimed invention.

Claim Rejections - 35 U.S.C. §103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

35 U.S.C. §103(a).

The *Graham* court set forth the factual inquiries that are applied for determining obviousness under 35 U.S.C. 103(a):

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 13-16, 19-20 are rejected under 35 U.S.C. 103(a) as obvious over Jain et al (2000, Metabolic engineering of an alternative pathway for ascorbic acid biosynthesis in plants, Molecular Biology 6:73-78) in view of Arner et al. (2001, Biochem J. 360:313-320).

Jain describes a method for reducing TSNAs in air cured tobacco, comprising the step of genetically engineering said tobacco (page 74, paragraph bridging col. 1 and 2) to include L-gulono- γ -lactone oxidase (GLOase, see abstract), wherein said step of genetically engineering said tobacco results in reduced levels of TSNAs in said tobacco, wherein said tobacco includes more than one copy of said gene, wherein said tobacco further includes a means to enhance transcription of said gene or genes (page 74, left column, 2nd Para.), wherein said step of

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genetically engineering said tobacco results in an increase in an endogenous level of vitamin C in said tobacco.

Jain also teaches that “[e]ven though plants and animals use different biosynthetic pathways to produce . . . [Vitamin C], it may be possible to . . . engineer plants to supplement their production of . . . [Vitamin C] using . . . components of the animal pathway.” Jain also teaches transgenic tobacco plants expressing an animal L-gulono- γ -lactone oxidase (GLOase) gene with increased Vitamin C. Jain also teaches that “expressing a novel gene in order to manipulate a biosynthetic pathway may be a useful approach to nutritional engineering to avoid problems with gene silencing and cosuppression”. (parag. bridging 76-77; abstract; page 73, rt. col. 2nd parag.).

Jain does not teach a myo-inositol oxygenase enzyme.

Arner teaches a myo-inositol oxygenase enzyme and suggests plants. (page 313, rt. col. 1st parag.; title , abstract)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the myo-inositol oxidase gene of Arner with the GLOase of Jain for the purposes of “engineer[ing] plants to supplement their production of . . . [Vitamin C].” One skilled in the art would have been motivated to generate the claimed invention because both genes are in the Vitamin C pathway and because “expressing a . . . gene . . . to manipulate a . . . pathway may be a useful approach to . . . avoid . . . gene silencing . . .” as taught by Jain. Jain’s success in increasing Vitamin C using GLOase would give the skilled artisan a reasonable expectation of success. Accordingly, the invention would have been obvious to one of ordinary skill in the art at the time of filing.

15. All Claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brendan O. Baggot whose telephone number is 571/272-5265. The examiner can normally be reached on Tuesday through Thursday, 10:00 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571/272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



ANNE MARIE GRUNBERG
SUPERVISORY PATENT EXAMINER